REMARKS/ARGUMENTS

Claims 1-3, 8-11, 13-14, and 16 are active in this application.

Claim 1 is amended to incorporate the definitions from Claim 15 and as a result Claim 15 is cancelled.

Claims 4-6 are cancelled obviating the objection noted at page 2 of the Action.

No new matter is added.

The pending claims in this application are directed to a multilayer dosage form of a pharmaceutical which includes a neutral core, an inner layer composed of a methacrylate polymer which itself is composed of particular (meth)acrylate monomers having particular properties, wherein the inner coating does not comprise plasticizer, a specified outer core, and an active bound to the polymer of the inner core. As discussed in the application in the paragraph bridging pages 5-6, this formulation provided initial slow release (due to the outer layer) followed by a similar slow release of the active that was not affected by the ionic strength of the dissolution medium.

In the Office Action, the Examiner has maintained the rejections in view of Ulmius (US 5,643,602) with or without Beckert et al (WO 01/68058). The reasons underlying the rejection remain largely the same as before.

The Office continues to misapprehend the evidentiary effect of unexpected results. In it's understanding, if it believes that it has made a *prima facie* case, no results provided by the invention could possibly be unexpected because they "flow naturally from following the suggestion of the prior art" (page 6 of the OA). In essence, the Office fails to understand the role of rebuttal evidence.

As the Office is well aware, it is legal error for the Office to dismiss a showing of unexpected results as flowing from or inherent in the Office prior art construct (in this case, the combination of Beckert and Ulmius). As stated in In re Sullivan, 84 USPQ2d 1034 (Fed. Cir. 2007):

> It is well settled that the PTO "bears the initial burden of presenting a prima facie case of unpatentability.... However, when a prima facie case is made, the burden shifts to the applicant to come forward with evidence and/or argument supporting patentability." *In re Glaug*, 283 F.3d 1335, 1338 (Fed. Cir. 2002). Rebuttal evidence is "merely a showing of facts supporting the opposite conclusion." *In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir. 1984). Evidence rebutting a prima face case of obviousness can include: "evidence of unexpected results," *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1369 (Fed. Cir. 2007), evidence "that the prior art teaches away from the claimed invention in any material respect," *In re Peterson*, 315 F.3d 1325, 1331 (Fed. Cir. 2003), and evidence of secondary considerations, such as commercial success and long-felt but unresolved needs, *WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1359 (Fed. Cir. 1999). When a patent applicant puts forth rebuttal evidence, the Board must consider that evidence. *See In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) (stating that "all evidence of nonobviousness must be considered when assessing patentability"); *In re Sernaker*, 702 F.2d 989, 996 (Fed. Cir. 1983) ("If, however, a patent applicant presents evidence relating to these secondary considerations, the board must always consider such evidence in connection with the determination of obviousness.").

Rather than considering Applicants' showing of unexpected results as rebuttal evidence to an alleged *prima facie* case, the Office has dismissed it and, in fact, has clearly convinced itself that unexpected results cannot exist when it thinks the Office has made a *prima facie* case. This is clear legal error.

In addition to their showing that there is no *prima facie* case, Applicants have shown an unexpected improvement in terms of the hypotonic/isotonic robust dissolution behavior. While Applicants do not concede that a skilled person would chose Eudragit® NE for the inner matrix from Ulmius and combine it with the outer Eudragit® FS coating of Beckert but even if that combination was appropriate, one skilled in the art would never expect the "hypotonic/isotonic" effect as has been so clearly demonstrated for the claimed invention.

The Office has put forth no reasoning that would support a conclusion that, *looking forward*, such an improvement would have been expected from the combination of Beckert and Ulmius. Rather, the Office looks backwards and concludes that because it is the Office's opinion that the references present a *prima facie* case any property, benefit, or characteristic of the invention Applicant wishes to discuss in rebuttal is meaningless. As the Office is aware, this is completely improper and, at best, is a classic case of requiring comparison of the results of the invention with the results of the invention. See MPEP 716.02(e) and *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966). On this point alone the rejection cannot be sustained.

As explained previously, even in view of WO 01/68767 (see pages 4-5 of the specification) that the claimed formulation provided these advantages was not predictable.

Further, as also discussed in the specification on page 5 and with respect to the added limitation to Claim 1 (previously Claim 15), it is advantageous to omit plasticizers in the inner coating, since it is always attempted to reduce excipients where ever possible in order to avoid or to reduce any interaction or incompatibilities with the active ingredient respectively risks for the patient. This is only possible when Eudragit® NE type polymers are used. When Eudragit® RL is used acceptable results (hypotonic/isotonic effect) are not achieved even in the absence of a plasticizer (see Fig. 6 of the present specification). Thus, the choice of Eudragit® NE type polymers (represented in the claims by the definition recited therein) was important to achieve this ability something not at all suggested by the cited art.

Ulmius (US 5,643,602) uses plasticizers throughout the examples (polysorbate 80 and acetyltributyl citrate). Ulmius mentions among the possible polymers for the inner coating Eudragit® NE but also Eudragit® RL which does not work (again see Fig. 6 of the present specification). Eudragit® RS which is very similar to Eudragit® RL can be expected to give the same unsatisfactory results. Except for Eudragit® NE, Eudragit® RS/RL and all the other

polymers mentioned by Ulmius in col.5., l.12 – 33, are not within the scope of the present claims. There is not a single example with Eudragit® NE in the inner coating. There is nothing said about the hypotonic/isotonic effect.

As noted above in In re Sullivan, another source of rebuttal evidence is "evidence 'that the prior art teaches away from the claimed invention in any material respect.'" In this case the Beckert teaches away from our present invention because the pharmaceutically active substance is placed onto the neutral core and not bound in the inner coating material as claimed. Beckert suggests to use an inner coating based on Eudragit® RS/RL which does not work as evidenced by the data presented in the specification. There is nothing said about the hypotonic/isotonic effect.

There is nothing in Ulmius and Beckert which provides the necessary direction to specifically select the type of metacrylate polymer defined in the claims from amongst all the possible polymers that are described by Ulmius (see listing in col. 5, for example). Second, that the selection of the specific methacrylate polymer permitted slow release of the active that was not affected by the ionic strength of the dissolution medium (see Examples in the application) could not have been predicted based on what Ulmius described (see page 5, last ¶ of the present application).

As explained in MPEP 2145: "An "obvious to try" rationale may support a conclusion that a claim would have been obvious where one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. " [A] person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1397 (2007).

However, as the evidence of record (in the specification) shows, reasonable prediction of success from the teachings of cited art are not present for the percentage release of active substance as defined in Claim 1 because the evidence shows that combinations within the teachings of Ulmius lead to compositions not meeting that definition. See also, *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd,* 533 F.3d 1353, 87 U.S.P.Q.2D 1452 (Fed. Cir. 2008): "To the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable."

To reiterate, Examples 5 and 6 in the present application illustrate the point made above. That is Example 5 employs Eudragit® NE 30 D as inner coat (that is meeting the definition provided in the claims) with an outer gastroresistant coating (Eudragit® L 30 D) whereas Example 6 uses an inner coat polymer Eudragit RL 30D, that is also described in Ulmius as a preferred polymer, see col. 5 and which does not meet the definition in the claims and having the same outer, gastroresistant coating (see page 33 of the specification). The release profiles of these two Examples are shown in FIGS 5 and 6 with FIG 5 showing the release profile of Example 5 in different ionic medium, isotonic or hypotonic and FIG 6 showing the same analysis for the material in Example 6.

As is clear from the figures, when the composition as defined in the claims was tested, the release profile remained relatively unchanged in the different ionic conditions, which was not the case for the composition in Example 6. Such an effect could not have been predicted based on what the art described (see page 5, last ¶ of the present application).

As the basis of the rejection is *prima facie* reasonable predictability and the evidence shows that this is not the case, it has not been established that the claims are obvious in view of the cited reference.

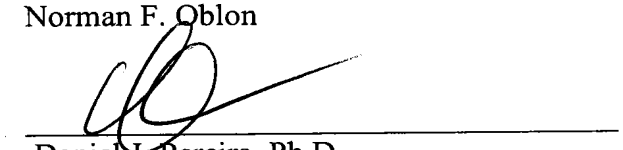
Further, the evidence rebuts any alleged *prima facie* case of obviousness, showing the improved results that the specification states would not have been reasonably predictable based on what is described in the cited art.

Withdrawal of the rejection is requested.

A Notice of Allowance is also requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Daniel J. Pereira, Ph.D.
Attorney of Record
Registration No. 45,518

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)

1687029_1.DOC